

(C) REMARKS

Reconsideration and withdrawal of all grounds of rejection are respectfully requested in view of the above amendments and following remarks. Claims 1-3, 6-10, 14 and 17-22 are pending herein. Claims 5, 11-13, 15 and 16 have been canceled hereby. New claims 17-22 have been added.

Referring to the rejection of the claims under 35 U.S.C. §112, in the independent claims, X, Y and Z have been restricted to hydrogen atoms in the formula representing the repeating units. Also, "n is at least 1" has been deleted from the independent claims. Applicants agree with the Office Action that the number of repeating units of the claimed polymer must be greater than 4, in accordance with common technical knowledge in the art of the word "polymer," compared to "oligomer" or "monomer" (for example, American Heritage Dictionary of the English language, Fourth Edition, 2000, referred to in the Office Action). If the Examiner believes it is necessary, despite Applicants' agreement with the Examiner's proffered meaning of "polymer" as having more than 4 repeating units, Applicants can amend the independent claims to specify a number of repeating units greater than 4.

In claim 6, "containing" has been amended to "consisting of," which sufficiently clarifies the claim.

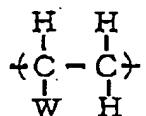
In claims 3, 9 and 10, "partially" has been deleted.

In claims 7-10, "comprising" has been amended to "consisting of." In particular, the Examiner recognized the invention recited in claim 7 as a "simple agent" without further explanation by Applicants. Nevertheless, to clarify claim 7 further it has been amended to recite "an agent adapted to prevent reconstruction of a blood vessel consisting of the functionalized polymer consisting of" the indicated repeating units.

In claim 9, "heparin/heparan sulfate" was amended to "heparin, heparan sulfate" to clarify the claimed invention.

1. Claims 1-3 and 7-16 were rejected on the grounds that they are anticipated by Tay et al. (Biomaterials, 1989, Vol. 10(1), pp. 11-15).

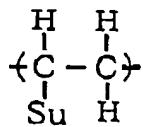
The present independent claims have been amended to recite that the invention features a polymer consisting of the following repeating units:



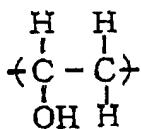
wherein, W denotes a carbohydrate chain including a structure corresponding to at least a portion of the basic skeletal structure of a glycosaminoglycan and comprising 2-50 constituent disaccharide units having an average of at least one sulfate group.

That is to say, the functionalized polymer of the present invention is a homopolymer consisting of homological repeating units and no other repeating units. As discussed above, the number of repeat units of the claimed polymer is greater than 4. The amended claims clarify that the invention is not directed to a monomer or oligomer, nor to a co-polymer having one or more repeating units without heparin, for example.

In contrast, the polymer disclosed in Tay et al. is a co-polymer, not a homopolymer as claimed. As described on page 4 of the Office Action, the polymers of Tay et al. include the following repeat unit of the following formula:



However, as explained in the Declaration by Mr. Hirofumi Yura, filed January 20, 2005, the polymers of Tay et al. must also include repeating units of the following formula, in light of the common knowledge in the art (please refer to the Declaration and the technical publications attached thereto):



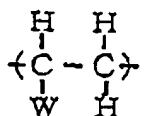
It appears that the Office Action concedes the conclusion of the Declaration by Mr. Yura that Tay et al. do not disclose a polymer in which every repeating unit necessarily contains a heparin moiety ("In the polymer of Tay even if all of the OH groups in the repeat unit of PVA are not substituted by heparins, there is at least one or more units in which the OH is substituted by heparin." Office Action, page 9.).

Moreover, Tay et al. do not inherently disclose a polymer with homologous repeating units having the recited carbohydrate chain W and no other repeating units. Rejections under §102 leave no room for speculation and require disclosure of all elements of the claimed invention either expressly or inherently. For there to be inherent anticipation, it must be clear that the features of the invention are consistently met each time when following the disclosure of the reference. There can be no experimentation, approximation or guesswork involved. "Inherent anticipation requires that the missing descriptive material is 'necessarily present,' not merely probably or possibly present, in the prior art." Trintec Indust., Inc. v. TOP-USA Corp., 63 USPQ2d 1597 (Fed. Cir. 2002), citing Continental Can Co. USA, Inc. v. Monsanto Co., 20 USQD2d 1746 (Fed. Cir. 1991). Applicants have shown that Tay et al. would not necessarily produce a polymer every time, in which each repeat unit has the recited carbohydrate moiety W.

In fact, Tay et al. teach away from increasing the density of heparin on the PVA chain. Tay et al. describe a substantial decrease of specific activity as the density of binding of heparin increases. (Page 14, right column, lines 5, 6). One of ordinary skill in the art following the teaching of Tay et al. would understand that the amount of heparin bound to the PVA must be decreased to increase specific activity. Therefore, the functionalized homo-polymer of the claimed invention is not anticipated or rendered obvious by the co-polymer disclosed in Tay et al. Accordingly, withdrawal of this rejection is respectfully requested.

2. Claims 1-3 and 7-16 were rejected as being anticipated by Larsson et al. (WO 93/05793).

Similar to Tay et al., Larsson et al. do not disclose a homo-polymer consisting of repeating units having the following structure:



Rather, Larsson et al. disclose a co-polymer (i.e., a polypeptide) comprising repeating amino acid units having a heparin side chain and repeating amino acid units without a heparin side chain. This is supported by the Mr. Yura's Declaration in which he points out that due to steric effects, the polymers of Larsson et al. would not have heparin on each repeating unit. In addition, the polymers of Larsson et al. are intended to provide antithrombin activity. Therefore, referring to the experimental data of Tay et al., one of ordinary skill in the art would avoid increasing heparin density along the polymer backbone. Also, Larsson et al. state that glycosaminoglycan residues should not be located so closely that they interfere with each other (page 9, lines 9-11). Moreover, the Declaration points out that Larsson et al. disclose that by selecting a polylysine having a molecular weight over 400,000, a synthetic proteoglycan having up to 500 heparin chains per carrier molecule may be prepared (page 14, lines 4-8). Since lysine monomer has a molecular weight of 128, a heparin chain exists per every 6.25 monomer units. Therefore, Larsson et al. do not anticipate or render obvious the claimed invention. Accordingly, withdrawal of this rejection is respectfully requested.

3. Claims 7-10, 12, 15 and 16 were rejected under 35 U.S.C. §102(b) in view of Joh (U.S. Patent 4,415,490).

Joh discloses non-thrombogenic material comprising a base polymer covalently bonded to heparin molecules. However, since the base polymers of Joh are functionalized by coupling a heparin to an aldehyde group on the base polymers, the

resulting polymers must be co-polymers comprising repeating units having a heparin molecule and repeating units without a heparin molecule. Accordingly, the polymers disclosed in Joh are different from the homo-polymer of the present invention.

In particular, the following discussion of Joh was provided in Mr. Yura's Declaration. Joh's non-thrombogenic materials are prepared by coupling heparin to the surface of an aldehyde-containing polymer film. The aldehyde-containing polymer film is prepared by surface treating a polymer film with periodic acid or lead tetra-acetate to cleave carbon-carbon bonds to give aldehyde groups on the surface of the polymer film. That is to say, Joh only discloses surface modification of a polymer film. The resulting non-thrombogenic materials of Joh have heparin activity only on their surfaces. Therefore, Joh does not anticipate or render obvious the claimed invention. Accordingly, withdrawal of this rejection is respectfully requested.

4. Claim 6 was rejected on the grounds that it is obvious in view of Conrad et al. (U.S. Patent 5,250,519) in combination with Joh.

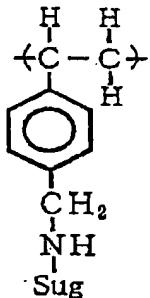
Conrad et al. disclose non-anticoagulant heparin derivatives, which allegedly show anti-proliferative activity with respect to smooth muscle cells. As conceded in the Office Action, Conrad et al. do not teach a cell growth control agent wherein a glycosaminoglycan is bound to a polymer backbone as in claim 1. As discussed above, the polymers of Joh are different than the inventive polymer. Therefore, one would not achieve the features of the claimed invention even, *assuming arguendo*, that the heparin molecules of Joh would have been replaced with the heparin derivatives of Conrad et al.

The attached technical publication co-authored by present inventors (M. Ishihara, K. Ono, K. Ishikawa, H. Hattori, Y. Saito, H. Yura, T. Akaike, Y. Ozecki, S. Tanaka, H. Mochizuki, A. Kurita, Enhanced Ability of Heparin-Carrying Polystyrene (HCPS) to Bind to Heparin-Binding Growth Factors and to Inhibit Growth Factor-Induced Endothelial Cell Growth, *J. Biochem.*, 127, 797-803 (2000)) discloses that a functionalized homo-polymer of the present invention (referred to in the paper as "hpHCPS") shows a remarkably excellent ability to inhibit the binding of growth factors to heparin beads, in comparison with a monomer (HCMS) and native heparin. That is to say, the present

invention of claim 6 provides a functional homo-polymer having an excellent effect for cell growth control.

New claims 17-22 further define the claimed invention from the applied references. Claims 17 and 18 depend from claims 6 and 7 respectively, and feature an agent wherein the functionalized polymer has a particular morphology in aqueous medium. Claim 19 depends on claim 6, and features an agent characterized in that the carbohydrate chain is a decomposed carbohydrate chain obtained by chemical decomposition of a natural glycosaminoglycan, and the decomposed carbohydrate chain is bonded to the polymer main chain via a functional group formed by the chemical decomposition. The applied references do not disclose or suggest the features of these claims in combination with the features of the main claims from which they depend.

Claims 20-22 depend from claims 1, 6 and 7, respectively, and feature the polymer having repeating units represented by the following formula:



wherein Sug indicates a structure corresponding to at least a portion of the basic skeletal structure of a glycosaminoglycan and comprising 2-50 constituent disaccharide units having an average of at least one sulfate group. It is not believed the applied references disclose or suggest the features of these claims (the moiety between the group Sug and the repeating unit of the polymer) in combination with the features of the main claims from which they depend.

It is respectfully submitted that the above amendments, taken in conjunction with the foregoing remarks, overcome all grounds of rejection. Accordingly, an early Notice of Allowance for all pending claims of the present application is respectfully requested.

Dated: August 11, 2005

Respectfully submitted,



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